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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Thomas M. Jessel Docket No.: 5199-169
Serial No.: 10/789,266 Examiner: to be assigned
Filed: February 26, 2004 Group Art Unit: 1636
Title: SYSTEMS AND METHODS FOR SCREENING FOR MODULATORS
OF NEURAL DIFFERENTIATION

January 12, 2005

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.97(b)

Sir:

In accordance with the duty of disclosure under 37 CFR §1.56, applicant hereby notifies the U. S. Patent and Trademark Office of the following documents, which are listed on the attached PTO/SB/08B form. The examiner may deem these documents to be relevant to patentability of the claims of the above-identified application.

The submission of the listed documents is not intended as an admission that any of the documents constitute prior art against the claims of the present application. Applicants do not waive any right to take any action that would be appropriate to antedate or otherwise remove any listed document as a competent reference against the claims of the present application.

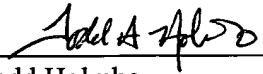
Applicants respectfully request that the listed documents be considered by the examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08B be returned in accordance with MPEP §609.

It is understood that no fee is necessary for submission of this Information Disclosure Statement, because it is being filed before the later of three months from the filing date or the mailing of the first Office Action on the merits.

BEST AVAILABLE COPY

The Commissioner is hereby authorized to charge payment of any fees associated with this application or credit any overpayment to Deposit Account No. 02-4270.

Respectfully submitted,



Todd Holmbo

Reg. No. 42,665

Attorney for Applicants

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PTO/SB/21 (08-03)

Approved for use through 08/30/2003. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

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**TRANSMITTAL
FORM**

(to be used for all correspondence after initial filing)

Total Number of Pages in This Submission

28

Application Number

10/789,266

Filing Date

02/26/04

First Named Inventor

Thomas M. Jessel

Art Unit

1636

Examiner Name

to be assigned

Attorney Docket Number

5199-169

ENCLOSURES (Check all that apply)

Fee Transmittal Form



Fee Attached



Amendment/Reply



After Final



Affidavits/declaration(s)



Extension of Time Request



Express Abandonment Request



Information Disclosure Statement

Certified Copy of Priority
Document(s)Response to Missing Parts/
Incomplete ApplicationResponse to Missing Parts
under 37 CFR 1.52 or 1.53

Drawing(s)



Licensing-related Papers



Petition

Petition to Convert to a
Provisional ApplicationPower of Attorney, Revocation
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Proprietary Information



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Todd Holmbo, Reg. No. 42,665

Signature

Date

01/12/05

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INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Complete if Known			
		Application Number	10/789,266		
		Filing Date	02/26/04		
		First Named Inventor	Thomas M. Jessel		
		Art Unit	1636		
		Examiner Name	to be assigned		
Sheet	1	of	25	Attorney Docket Number	5199-169

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Abbondanzo et al., Derivation of embryonic stem cell lines.	
		Methods Enzymol., 225: 803-823, 1993	
		Akhurst and Derynck, TGF-beta signaling in cancer-a double-edged sword.	
		Trends Cell Biol., 11(11): S44-51, 2001	
		Alvarez-Buylla et al., A unified hypothesis on the lineage of neural stem cells.	
		Nat. Rev. Neurosci., 2: 287-293, 2001	
		Arber et al., Requirement for the homeobox gene Hb9 in the consolidation of motor neuron identity.	
		Neuron, 23: 659-764, 1999	
		Bain et al., Embryonic stem cells express neuronal properties in vitro.	
		Dev. Biol., 168: 342-357, 1995	

Examiner Signature		Date Considered	
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*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

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Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary)		Complete if Known			
		Application Number	10/789,266		
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		First Named Inventor	Thomas M. Jessell		
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Sheet	2	of	25	Attorney Docket Number	5199-169

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		Bak et al., The Hedgehog signaling pathway – implications for drug targets in cancer and neurodegenerative disorders.	
		Pharmacogenomics, 4(4): 411-429, 2003 (N/A)	
		Beers and Berkow, eds., The Merck Manual of Diagnosis and Therapy, 17th ed. Whitehouse Station, NJ: Merck Research Laboratories, 1999, chap. 183	
		Belting et al., Multiple phases of expression and regulation of mouse Hoxc8 during early embryogenesis.	
		J. Exp. Zool., 282: 196-222, 1998	
		Bieri et al., Abnormal nerve conduction studies in mice expressing a mutant form of the POU transcription factor, SCIP.	
		J. Neurosci. Res., 50:821-828, 1997	
		Bloch-Gallego et al., Survival in vitro of motoneurons identified or purified by novel antibody-based methods is selectively enhanced by	
		muscle-derived factors.	
		Development, 111: 221-232, 1991	

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		Art Unit	1636
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Sheet 3	of 25	Attorney Docket Number	5199-169

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		Blumberg et al., An essential role for retinoid signaling in anteroposterior neural patterning.	
		Development, 124: 373-379, 1997	
		Botchkarev, V.A., Bone morphogenetic proteins and their antagonists in skin and hair follicle biology.	
		Journal of Investigative Dermatology, 120: 36-47, 2003	
		Brazelton et al., From marrow to brain: expression of neuronal phenotypes in adult mice.	
		Science, 290: 1775-1779, 2000	
		Briscoe and Ericson, Specification of neuronal fates in the ventral neural tube.	
		Curr. Opin. Neurobiol., 11: 43-49, 2001	
		Briscoe et al., A homeodomain protein code specifies progenitor cell identity and neuronal fate in the ventral neural tube.	
		Cell, 101: 435-445, 2000	

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		Byrd et al., Hedgehog is required for murine yolk sac angiogenesis.	
		Development, 129: 361-372, 2002	
		Cadigan and Nusse, Wnt signaling: a common theme in animal development.	
		Genes Dev., 11(24): 3286-3305, 1997	
		Camu et al., Purification of embryonic rat motoneurons by panning on a monoclonal antibody to the low-affinity NGF receptor.	
		J. Neurosci. Methods, 44: 59-70, 1992	
		Chambon, P., The molecular and genetic dissection of the retinoid signaling pathway.	
		Recent Prog. Horm. Res., 50: 317-332, 1995	
		Chambon, P., The retinoid signaling pathway: molecular and genetic analysis.	
		Semin. Cell Biol., 5(2): 115-125, 1994	

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		Art Unit	1636
		Examiner Name	to be assigned
Sheet 5	of 25	Attorney Docket Number	5199-169

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		Chiang et al., Cyclopia and defective axial patterning in mice lacking Sonic hedgehog gene function.	
		Nature, 383: 407-413, 1996	
		Chiba et al., Distinct retinoid X receptor – retinoic acid receptor heterodimers are differentially involved in the control of expression of	
		of retinoid target genes in F9 embryonal carcinoma cells.	
		Mol. Cell Biol., 17: 3013-3020, 1997	
		Choi et al., A generic intron increases gene expression in transgenic mice.	
		Mol. Cell Biol., 11: 3070-3074, 1991	
		Cross and Claesson-Welsh, FGF and VEGF function in angiogenesis: signaling pathways, biological responses and therapeutic inhibition.	
		Trends Pharmacol. Sci., 22(4): 201-207, 2001	

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		First Named Inventor	Thomas M. Jessel		
		Art Unit	1636		
		Examiner Name	to be assigned		
Sheet	6	of	25	Attorney Docket Number	5199-169

NON PATENT LITERATURE DOCUMENTS			
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		Danielsen and Maihle, The EGF/ErbB receptor family and apoptosis.	
		Growth Factors, 20(1): 1-15, 2002	
		Davis and Joyner, Expression patterns of the homeobox-containing genes En-1 and En-2 and the proto-oncogene int-1 diverge during	
		mouse development.	
		Genes Dev., 2: 1736-1744, 1988	
		Durston et al., Retinoids and related signals in early development of the vertebrate central nervous system.	
		Curr. Top. Dev. Biol., 40: 111-175, 1998 (N/A)	
		Dyer et al., Indian hedgehog activities hematopoiesis and vasculogenesis and can respecify prospective neurectodermal cell fate in the mouse embryo.	
		Development, 128: 1717-1730, 2001	

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		Ericson et al., Pax6 controls progenitor cell identity and neuronal fate in response to graded SHh signaling.	
		Cell, 90: 169-180, 1997	
		Ericson et al., Two critical periods of Sonic Hedgehog signaling required for the specification of motor neuron identity.	
		Cell, 87: 661-673, 1996	
		Falls, D.L., Neuregulins: functions, forms, and signaling strategies.	
		Exp. Cell Res., 284(1) 14-30, 2003	
		Frank-Kamenetsky et al., Small-molecule modulators of Hedgehog signaling: Identification and characterization of Smoothed agonists and antagonists.	
		J. Biol. 1(2): 10, 2002	
		Gage, F. H., Mammalian neural stem cells.	
		Science, 287: 1433-1438, 2000	

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		Giles et al., Caught up in a Wnt storm: Wnt signaling in cancer.	
		Biochim. Biophys. Acta., 1653(1): 1-24, 2003	
		Goodwin and D'Amore, Wnt signaling in the vasculature.	
		Angiogenesis, 5(1-2): 1-9, 2002 (N/A)	
		Gratsch et al., Noggin and chordin have distinct activities in promoting lineage commitment of mouse embryonic stem (ES) cells.	
		Dev. Biol., 245: 83-94, 2002 (N/A)	
		Hatsell et al., Beta-catenin and Tcfs in mammary development and cancer.	
		J. Mammary Gland Biol. Neoplasia., 8: 145-158, 2003	
		Hollyday et al., An autoradiographic study of the formation of the lateral motor column in the chick embryo.	
		Brain Res., 132: 197-208, 1977	

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Sheet 9	of 25	Attorney Docket Number	5199-169

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		Hsieh et al., Biochemical characterization of Wnt-frizzled interactions using a soluble, biologically active vertebrate Wnt protein.	
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		Application Number	10/789,266
		Filing Date	02/26/04
		First Named Inventor	Thomas M. Jessel
		Art Unit	1636
		Examiner Name	to be assigned
Sheet 10 of 25	Attorney Docket Number	5199-169	

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		Kalderon, D., Hedgehog signaling: Costal-2 bridges the transduction gap.	
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		Lauta, V. M., A review of the cytokine network in multiple myeloma: diagnostic, prognostic, and therapeutic implications.	
		Cancer, 97(10): 2440-2452, 2003	
		Lee et al., Transcriptional networks regulating neuronal identity in the developing spinal cord.	
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		Mezey et al., Turning blood into brain: cells bearing neuronal antigens generated in vivo from bone marrow.	
		Science, 290: 1779-1782, 2000	

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		Miyazono et al., Divergence and convergence of TGF-beta/BMP signaling.	
		J. Cell Physiol., 187(3): 265-276, 2001	
		Miyazono, K., Positive and negative regulation of TGF-beta signaling.	
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		Muhr et al., Convergent inductive signals specify midbrain, hindbrain, and spinal cord identity in gastrula stage chick embryos.	
		Neuron, 23: 689-702, 1999	
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		Novitch et al., Coordinate regulation of motor neuron subtype identity and pan-neuronal properties by the bHLH repressor Olig2.	
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		Development, 130(22): 5297-5305, 2003	

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		O'Brien et al., Development and survival of thoracic motoneurons and hindlimb musculature following transplantation of the thoracic neural tube	
		to the lumbar region in the chick embryo: anatomical aspects.	
		J. Neurobiol., 21: 313-340, 1990	
		Ornitz and Itoh, Fibroblast growth factors.	
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		Pevny et al., Generation of purified neural precursors from embryonic stem cells by lineage selection.	
		Curr. Biol., 8: 971-974, 1998	
		Pfaff et al., Requirement for LIM homeobox gene Isl1 in motor neuron generation reveals a motor neuron-dependent step in interneuron differentiation.	
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		Povelones and Nusse, Wnt signaling sees spots.	
		Nat. Cell Biol., 4(11): E249-250, 2002	

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		Raju et al., SANE, a novel lem domain protein, regulates bone morphogenetic protein signaling through interaction with smad1.	
		J. Biol. Chem., 278(1): 428-437, 2003	
		Rathjen et al., Directed differentiation of pluripotent cells to neural lineages: homogenous formation and differentiation of a neurectoderm population.	
		Development, 129: 2649-2661, 2002	
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		Mech. Dev., 79: 185-197, 1998	
		Reubinoff et al., Neural progenitors from human embryonic stem cells.	
		Nat. Biotechnol., 19: 1134-1140, 2001	
		Ring and Cho, Specificity in transforming growth factor- beta ^{beta} signaling pathways.	
		Am. J. Hum. Genet., 64: 691-697, 1999	

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		Roelink et al., Floor plate and motor neuron induction by different concentrations of the amino-terminal cleavage product of sonic hedgehog	
		autoproteolysis.	
		Cell, 81: 445-455, 1995	
		Sander et al., Ventral neural patterning by Nkx homeobox genes: Nkx6.1 controls somatic motor neuron and ventral interneuron fates.	
		Genes Dev., 14: 2134-2139, 2000	
		Schuldiner et al., Induced neuronal differentiation of human embryonic stem cells.	
		Brain Res., 913: 201-205, 2001	
		Sharma et al., Genetic and epigenetic mechanisms contribute to motor neuron pathfinding.	
		Nature, 406: 515-519, 2000	

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		Sharma et al., LIM homeodomain factors Lhx3 and Lhx4 assign subtype identities for motor neurons.	
		Cell, 95: 817-828, 1998	
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		Application Number	10/789,266		
		Filing Date	02/26/04		
		First Named Inventor	Thomas M. Jessel		
		Art Unit	1636		
		Examiner Name	to be assigned		
Sheet	20	of	25	Attorney Docket Number	5199-169

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
		Terada et al., Bone marrow cells adopt the phenotype of other cells by spontaneous cell fusion.	
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		First Named Inventor	Thomas M. Jessel		
		Art Unit	1636		
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		Uchida et al., Direct isolation of human central nervous system stem cells.	
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		Vallstedt et al., Different levels of repressor activity assign redundant and specific roles to NKx6 genes in motor neuron and interneuron specification.	
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		Waxman and Bennett, Relative conduction velocities of small myelinated and nonmyelinated fibres in the central nervous system.	
		Nature New Biol., 238:217, 1972	
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		Curr. Biol., 10: 421- 429, 2000	

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		Wilson et al., Neural induction: toward a unifying mechanism.	
		Nat. Neurosci., 4 Suppl.: 1161-1168, 2001	
		Wilson et al., The status of Wnt signaling regulates neural and epidermal fates in the chick embryo.	
		Nature, 411: 325-330, 2001	
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		Wrana, J., Regulation of Smad activity. Cell, 100: 189-192, 2000	
		Xian et al., Peering into early neurogenesis with embryonic stem cells.	
		Trends Neurosci., 24: 685-686, 2001	

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		Yamada et al., Control of cell pattern in the developing nervous system: polarizing activity of the floor plate and notochord.	
		Cell, 64: 635-647, 1991	
		Yamaguchi et al., XIAP, a cellular member of the inhibitor of apoptosis protein family, links the receptors to TAB1-TAK1 in the BMP signaling pathway.	
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		Nature, 416: 545-548, 2002	
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		Nat. Biotechnol., 19: 1129-1133, 2001	

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		Zhou et al., The bHLH transcription factors OLIG2 and OLIG1 couple neuronal and glial subtype specification.	
		Cell, 109: 61-73, 2002	
		Liu et al., Assigning the positional identity of spinal motor neurons. Rostrocaudal patterning of Hox-c expression by FGFs, Gdf11, and	
		retinoids.	
		Neuron, 32: 997-1012, 2001	
		Wichterle et al., Directed differentiation of embryonic stem cells into motor neurons.	
		Cell, 110: 385-397, 2002	

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